Amendments to the Specification

Please replace the Substitute "Sequence Listing" mailed to the United States Patent and Trademark Office on June 1, 2004 (sheets 1/3 through 3/3) with the Substitute "Sequence Listing" (sheets 1/4 through 4/4) comprising SEQ ID NOs 1 through 9 filed concurrently herewith.

Please replace the paragraph at page 3, line 24 through page 4, line 26 with the following amended paragraph:

NPAR agonists include thrombin derivatives described in U.S. Patent Nos. 5,352,664 and 5,500,412. For example, a thrombin peptide derivative can comprise a thrombin receptor binding domain having the L-amino acid sequence Arg-Gly-Asp-Ala (SEQ ID NO: 7), and a serine esterase conserved sequence. In on embodiment, a peptide derivative of thrombin comprises a serine esterase conserved sequence, Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val (SEQ ID NO: 8). One example of an NPAR agonist is a thrombin peptide derivative, i.e., a polypeptide with less than about fifty amino acids, preferably less than about thirty-three amino acids and having sufficient homology to the fragment of human thrombin corresponding to prothrombin amino acids 508-530 (Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val: SEQ ID NO.: 1) that the polypeptide activates NPAR. The thrombin peptide derivatives described herein preferably have between about 14 and 23 amino acids, more preferably between about 19 and 23 amino acids. Optionally, the thrombin peptide derivatives described herein can be amidated at the *C*-terminus and/or acylated at the *N*-terminus. In one embodiment, the thrombin peptide derivative being administered to the chronic ~~dermal~~ skin ulcer has the following amino acid sequence: R1-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2: SEQ ID NO.: 5. R1 is -H or R3-C(O)-; R2 is -OH or -NR4R5; R3 is -H or C1-C6 alkyl group (preferably $-CH_3$); and R4 and R5 are independently -H, C1-C6 alkyl group or, taken together with the nitrogen atom to which they are bonded, are a non-aromatic heterocyclic group such a piperidinyl, morpholinyl,

thiomorphinyl or pyrollidinyl (preferably R4 and R5 are both -H). Preferably R1 is -H and R2 is $-NH_2$; or R1 is -H and R2 is -OH. Alternatively, the thrombin peptide derivative being administered to the chronic skin ulcer has the amino acid sequence of SEQ ID NO.: 3: R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-Met-Lys-Ser-Pro-Phe-R2. R1 and R2 are as described above. It is understood, however, that zero, one, two or three amino acids at positions 1-9 and 14-23 in the thrombin peptide derivative can differ from the corresponding amino acid in SEQ ID NO.: 5. It is also understood that zero, one, two or three amino acids at positions 1-14 and 19-33 in the thrombin peptide derivative can differ from the corresponding amino acid in SEQ ID NO.: 3. Preferably, the amino acids in the thrombin peptide derivative which differ from the corresponding amino acid in SEQ ID NO.: 3 or SEQ ID NO.: 5 are conservative substitutions, and are more preferably highly conservative substitutions. Alternatively, an *N*-terminal truncated fragment of the thrombin peptide derivatives having at least fourteen amino acids or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids can be contacted with the chronic ~~dermal~~ skin ulcer.

Please add the following new paragraphs at page 4, line 27, immediately prior to the paragraph at page 4, line 27 to page 5, line 3:

A thrombin receptor binding domain is defined as a polypeptide sequence which directly binds to the thrombin receptor and/or competitively inhibits binding between high-affinity thrombin receptors and alpha-thrombin.

A domain having a serine esterase conserved sequence comprises a polypeptide sequence containing at least 4-12 of the N-terminal amino acids of the dodecapeptide previously shown to be highly conserved among serine proteases (Asp-X_1-Cys-X_2-Gly-Asp-Ser-Gly-Gly-Pro-X_3-Val; SEQ ID NO: 9); wherein X_1 is either Ala or Ser; X_2 is either Glu or Gln; and X_3 is either Phe, Met, Leu, His, or Val).

Please replace the paragraph at page 9, line 22 through page 10, line 9 with the following amended paragraph:

This study was a multi-center, randomized, double blind, three-arm Phase IIa pilot study evaluating synthetic thrombin peptide TP508 for accelerating the healing of chronic diabetic ulcers. Patients were randomized to one of three topical treatment groups: 1 microgram of TP508 in saline applied twice weekly, 10 micrograms of TP508 in saline applied twice weekly, or saline placebo applied twice weekly. All patients received a ~~regiment~~ regimen of standard diabetic ulcer care consisting of initial sharp debridement, wound cleansing, wound dressing, and wound pressure offloading. Wounds were evaluated twice a week for up to 20 weeks or until wound closure, whichever was earlier. Patients were removed from the study if they developed a clinical infection or if the wound condition significantly deteriorated. At each wound evaluation (twice weekly), the wound perimeter was traced for determination of wound area, and the wound was photographed with a digital camera. Blood chemistry and hematology tests were performed at patient enrollment, and at weeks 5, 10, 15, and 20. A radiographic assessment was conducted every 5 weeks to study effects on underlying bone composition.